CLAIM + DETAILED DESCRIPTION

[Claim(s)]
[Claim 1] Skin external preparations characterized by containing [the acylation derivative of glycosyl L-ascorbic acid] 0.1 to 60.0 weight % for 0.001 to 10.0 weight %, and silicone oil.
[Claim 2] Skin external preparations according to claim 1 whose glycosyl L-ascorbic acid of a glycosyl L-ascorbic acid acylation derivative is 2-glucopyranosyl L-ascorbic acid or 2-galactopyranosyl L-ascorbic acid.
[Claim 3] Skin external preparations according to claim 1 or 2 whose acyl group in a glycosyl L-ascorbic acid acylation derivative is what makes a basic skeleton lower fatty acid or a higher fatty acid.
[Claim 4] Skin external preparations according to claim 1 to 3 which are the integer as which the carbon number of the acyl group in a glycosyl L-ascorbic acid acylation derivative is chosen from 3 to 20.
[Claim 5] Skin external preparations according to claim 1 to 4 whose glycosyl L-ascorbic acid acylation derivative is a mono-acylation derivative.
[Claim 6] Skin external preparations according to claim 1 to 5 with which the hydroxyl of the position of the 6th place of the glycosyl L-ascorbic acid residue of a glycosyl L-ascorbic acid acylation derivative is acylated.
[Claim 7] Skin external preparations according to claim 1 whose silicone oil is the thing of viscosity 6 - 100cSt.

[Detailed Description of the Invention]
[0001]
[Field of the Invention] Especially this invention relates to the skin external preparations which have the using feeling which skin familiarity was good and felt refreshed about skin external

preparations.

[0002]

[Description of the Prior Art] As recent years, stability, and an oil-soluble ascorbic acid derivative The acylation derivative of glycosyl L-ascorbic acid which is the substance in which sugar and fatty acid carried out coordination to the 2nd place of ascorbic acid and the 6th place, respectively is reported (the collection 3 of the 118th annual convention lecture summaries of the Pharmaceutical Society of Japan, 77 pages, Heisei 10(1998) March 5 issue). With the esterase activity and glucosidase activity in epidermis and dermis, the acylation derivative of this glycosyl L-ascorbic acid produces L-ascorbic acid, when the amount of [a fatty acid portion and] sugar part dissociates. the dopa quinone whose L-ascorbic acid is generally the metabolic turnover intermediate product of melanin generation process, or dopa -- returning chromium to dopa It has the operation which returns the dark color oxidation type melanin which is controlling and generating melanin generation to light color reduction type melanin, and is a compound effective in the therapy of whitening-izing of the skin, a stain, a freckle, the melasma, the chloasma, etc., and an improvement. Since the acylation derivative of glycosyl L-ascorbic acid does not have a reducibility machine in intramolecular if the acylation derivative of glycosyl L-ascorbic acid is compared with L-ascorbic acid, To heat, light, oxygen, and a metal ion, it is stable and excels in the point that the increase of oil solubility and percutaneous absorption are improved by addition of fatty acid.

[0003] However, the skin external preparations which blended the acylation derivative of this glycosyl L-ascorbic acid have a characteristic feeling of stickiness, and it had the fault that feels, such as a cosmetic which blended this, worsened. For this reason, the acylation derivative of glycosyl L-ascorbic acid could be blended, moreover it was sticky and skin external preparations with little admiration, especially a skin cosmetic were desired.

[0004]

[Means for Solving the Problem] In order to solve said technical problem, as a result of inquiring wholeheartedly, by using combining the acylation derivative and silicone oil of glycosyl L-ascorbic acid, this invention person etc. finds out that a characteristic feeling of stickiness is reduced, and came to complete this invention.

[0005] That is, this invention is skin external preparations characterized by containing [the acylation derivative of glycosyl L-ascorbic acid] 0.1 to 60.0 weight % for 0.001 to 10.0 weight %, and silicone oil.

[0006]

[Embodiment of the Invention] Below, the form of operation of this invention is explained in detail. With glycosyl L-ascorbic acid as used in the field of this invention, all the glycosyl L-ascorbic acid by which oil solubility is improved by acylation is included. As desirable glycosyl L-ascorbic acid 1, two or more glucosyl residues, or a galactosyl residue combined with the

position of the 2nd place in L-ascorbic acid. For example, a series of 2-glucopyranosyl L-ascorbic acid including 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, And a series of 2-galactopyranosyl L-ascorbic acid including 2-O-beta-D-mono-galactopyranosyl L-ascorbic acid is mentioned.

[0007] Acylation as used in the field of this invention means introducing acyl group RCO- into this glycosyl L-ascorbic acid. Here, R means the alkyl group of the saturation which usually makes a carbon number 2 to 19, and the integer desirably chosen from 4 to 17, or unsaturation which has the shape of a normal chain, or branching. [derivative / therefore, / as used in the field of this invention / acylation] Although the compound at large which the acyl group combined with 1 or two or more hydroxyls of 1 or two or more hydroxyls in glycosyl L-ascorbic acid like the above-mentioned, and a L-ascorbic acid residue [in / desirably / glycosyl L-ascorbic acid] will be meant It is a mono-acylation derivative especially preferably.

[0008] This acylation derivative can be prepared by a variety of method. For example, if a proper acylating agent is made to react to glycosyl L-ascorbic acid, a desired acylation derivative will be obtained. As long as it is with necessity at this time, a catalyst may be made to live together in the system of reaction, and that catalyst may be enzymes, such as lipase. [glycosyl L-ascorbic acid used as a raw material] For example, as indicated to JP,H3-139288,A, JP,H3-135992,A, and JP,H3-183492,A [make / alpha-glucosyl compounds, such as cyclo malto dextrin and an amylolysis thing / to react to L-ascorbic acid under existence of glycosyltransferases, such as cyclo malto dextrin glucanotransferase,] Or as indicated to JP,H6-228183,A and JP,H6-263790,A It can obtain by making beta-galactosyl compounds, such as lactose, react to 5 and 6-isopropylidene L-ascorbic acid under existence of the beta-galactosidase. Incidentally as a commercial item of 2-glucopyranosyl L-ascorbic acid, "AA-2G" (98% or more of the 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid content per solid content weight, Hayashibara Trading company Sale) is mentioned, for example. Although based also on a use, you may be a mixture with other components which glycosyl L-ascorbic acid is not necessarily highly refined in this invention, and do not bar substantial acylation even if ** is also good and it is a non-dissociated constituent with an analog and other components peculiar to the preparation methods.

[0009] When based on a chemical reaction, as each method, the method of using acylating agents, such as an acid or acid halide, acid anhydride, or acid ester, is mentioned, for example that what is necessary is just to usually apply the general method for acylating the compound which has hydroxyl. as an acylating agent -- usually -- 3 to 20 -- desirably The propionic acid which makes a carbon number the integer chosen from 4 to 18, Butanoic acid, isobutyric acid, n-valerianic acid, isovaleric acid, trimethylacetic acid, Caproic acid, n-oenanthic acid, caprylic acid, pelargonic acid, capric acid, Lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid, Oleic acid, ricinoleic acid, arachidic acid, a petroselinic acid, a vaccenic acid,

Carboxylic acid and the carboxylic acid halide, the carboxylic anhydride, and carboxylate which make a basic skeleton lower fatty acid and higher fatty acids, such as linolic acid, linolenic acid, eleostearic acid, licanic acid, parinaric acid, a tariric acid, the Kad Laing acid, and arachidonic acid, are used.

[0010] A reaction is usually performed by the non-basin system which intercepted invasion of the water to the system of reaction. For example, the inside of organic solvents, such as pyridine, dimethyl sulfoxide, and dimethylformamide, Make catalysts, such as p-toluenesulfonic acid, live together, and a carboxylic anhydride is made to react to glycosyl L-ascorbic acid if needed, or carboxylic acid itself is made to react to glycosyl L-ascorbic acid under existence of the catalyst of concentrated sulfuric acid etc. Although the reaction usually used for acylation of L-ascorbic acid can apply as it is as a reaction condition When making 3mol or less of acylating agents [2mol or less of] react desirably to 1mol of glycosyl L-ascorbic acid, a reaction advances almost specifically and an acyl group can be introduced into the specific part of the L-ascorbic acid residue in glycosyl L-ascorbic acid. For example, if an acylating agent of 2mol or less is made to react in the case of 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, only the hydroxyl of the position of the 6th place in a L-ascorbic acid residue can be acylated substantially. Moreover, after acylating only the hydroxyl of the 6th place in L-ascorbic acid by a well-known method, Among the proper mixture of an organic solvent or an organic solvent, and water, suitably for example When making alpha-glucosyl compounds, such as cyclo malto dextrin and a starch partial hydrolysate, react to the acylated L-ascorbic acid under existence of glycosyltransferases, such as cyclo malto dextrin glucanotransferase The mono-acylation derivative of 2-glucopyranosyl L-ascorbic acid with which only the hydroxyl of the 6th place in a L-ascorbic acid residue was acylated can be obtained.

[0011] When based on an enzyme reaction, glycosyl L-ascorbic acid and an acylating agent are used as a substrate, the proper organic solvent according to these substrates and enzymes is used, and the binary system which consists of the water and the organic solvent of a partition ratio suitably depending on the case is usually used. As an enzyme, lipase is common and the enzyme agent may be fixed. As an organic solvent, hydrophilic organic solvents, such as sec-butyl alcohol, t-butyl alcohol, t-amyl alcohol, dioxane, tetrahydrofuran, diethylether, dichloromethane, and pyridine, are used, for example. There is no restriction also in particular in the kind of enzyme that what is necessary is just to set up a reaction condition like the case of acylation of L-ascorbic acid by enzymatic process. In addition, since glycosyl L-ascorbic acid, division, and 2-glucopyranosyl L-ascorbic acid have the remarkably high stability in an aqueous solution, unlike the case of acylation of L-ascorbic acid, they do not have the necessity for a complicated condition setup.

[0012] The acylation derivative obtained in this way can be refined by applying the usual method for refining fatty acid ester of L-ascorbic acid. As each refining method, for example

Salting out, a dialysis, filtration, concentration, fractional precipitation, Liquid separation extraction, gel chromatography, exchange chromatography, High performance chromatography, gas chromatography, affinity chromatography, gel electrophoresis, isoelectric focusing, crystallization, etc. are mentioned, and according to the kind and purity of a reaction condition and the acylation derivative for which it asks, these are combined suitably and applied.

[0013] The acylation derivative of glycosyl L-ascorbic acid used by this invention has many following character.

(1) As compared with L-ascorbic acid or well-known inorganic acid ester, oil solubility is high. And substantial water solubility can be held, giving oil solubility, when adjusting the chain length of the alkyl group in an acylating agent.

(2) Since L-ascorbic acid is separated in the living body unlike well-known fatty acid ester or inorganic acid ester, the physiological function of L-ascorbic acid original can be expected, and safety is also high.

(3) Unlike L-ascorbic acid, it is very stable to heat, light, oxygen, and a metal ion.

(4) Since direct reduction nature is not shown unlike L-ascorbic acid, don't cause a reaction like a Maillard reaction, for example.

(5) Unlike L-ascorbic acid or well-known inorganic acid ester, the permeability of the skin or membrane is high.

(6) There is character which catches the radical generated in the living body as well as L-ascorbic acid.

(7) Although based also on the kind of acylating agent, or the grades of refining, generally they are tasteless, a non-smell, and colorlessness.

[0014] [the acylation derivative used by these character, therefore this inventions] In the skin external preparations containing the cosmetics and drugs which need the physiological function of L-ascorbic acid original It is made stability, and can use advantageously as a safe L-ascorbic acid source of supply, and, in addition to a whitening operation, the function to protect the skin from the free radical which happens by UV irradiation, the function which activates skin cells, the function which prevents optical hindrance, the function which raises skin immunity, etc. are expected. Since the permeability to the skin or membrane is remarkably high, the acylation derivative which the acyl group which makes a carbon number the acylation derivative which comparatively long chain length's acyl group combined also among the acylation derivatives used by this invention, division, and eight or more integers combined is useful especially in the field of cosmetics or drugs.

[0015] As an example of the acylation derivative of the glycosyl L-ascorbic acid used by this invention For example, 6-O-butyryl 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, 2-O-alpha-D-mono-glucopyranosyl 6-O-hexa noil L-ascorbic acid, 2-O-alpha-D-mono-

glucopyranosyl 6-O-octanoyl L-ascorbic acid, 6-O-decanoyl 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, 6-O-dodeca noil 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, 6-O-myristoyl 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid, 6-O-palmitoyl 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid or 6-O-stearoyl 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid is mentioned.

[0016] The loadings of the glycosyl L-ascorbic acid acylation derivative in this invention are 0.01 to 5.0 weight % preferably 0.001 to 10.0weight %. At less than 0.001 weight %, while the effect according to the combination purpose of the glycosyl L-ascorbic acid acylation derivative is hard to be demonstrated, since smeariness may be produced in respect of usability when it is inferior to skin familiarity and 10.0 weight % is exceeded, it is not desirable.

[0017] Any are sufficient as long as it is the organic silicon compound which has a siloxane bond as silicone oil used by this invention, for example. A methylpolisiloxane, dimethylpolysiloxane, methylphenyl polysiloxane, methil hydrogen polysiloxane, decamethyl cyclopentasiloxane, octamethylcyclotetrasiloxane, a polyoxyethylene methylpolisiloxane copolymer, etc. are mentioned.

[0018] The thing of about 6-100 cSt is suitable for the viscosity of the silicone oil used by this invention. Since the feeling of smeariness of the acylation derivative of hypoviscosity past ** and glycosyl L-ascorbic acid cannot be pressed down and hyperviscous past ** and silicone oil itself may produce smeariness, it is not desirable.

[0019] 0.1 to 60.0 weight % is suitable for the loadings of the silicone oil used by this invention. When there are too few loadings of silicone oil, even if it cannot fully press down smeariness of external preparations and is too large more than needed, skin familiarity may worsen and it is not desirable.

[0020] Components, such as the surface active agent, the oil and the moisturizer which are generally used for cosmetics, quasi drugs, etc., an ultraviolet ray absorbent, alcohols, a chelating agent, antiseptics, a thickener, a pigment, and perfume, can be blended with the skin external preparations of this invention.

[0021] The skin external preparations of this invention can be manufactured by the usual method, for example, can be applied as a basic cosmetic, a medicinal cosmetic, an external use physic base, etc.

[0022]

[Example] Although a work example and a comparative example explain this invention in more detail below, thereby, this invention is not limited. In addition, all the loadings shown below are weight %.

[0023] The milky lotion of the presentation shown in Table 1 of a work example 1 and the 1-3rd comparative examples was prepared with the conventional method, and it was considered as a work example 1 and comparative examples 1-3. The manufacture method of the 2-O-alpha-D-

mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid used in the work example etc. is as after-mentioned. Moreover, the using feeling was evaluated by the method of carrying out a postscript about each obtained sample. The result is combined and is shown in Table 1.

[0024] (1) Under the manufacture method room temperature of 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid, a reaction container -- 2-glucopyranosyl L-ascorbic acid (a trade name "AA-2G" --) Until it takes 98% or more of the 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid content per solid content weight, and 2.71g (8.0mmol) of stock meeting woods Hayashibara trading company sale, it adds 350ml of pyridine under an argon air current and it dissolves It agitated. Next, the caprylic anhydride (9.6mmol) dissolved in pyridine 50ml was poured between the bottom of an argon air current, and dichotomy, and it was made to react for 165 minutes under ********** and a room temperature into a reaction container. Then, in the reaction container, methanol was added and condensed, it hardened by drying, and the reaction was stopped.

[0025] The solid state material of the obtained reaction mixture (4.65g) Load is carried out to a silica gel [for column chromatography / 139.5g] (a trade name "WAKOGERU", WAKO PURE CHEMICAL INDUSTRIES LTD. manufacture) column. 500ml of ethyl acetate, 500ml of ethyl acetate / methanol mixture (capacity factor 9:1), While dipping ethyl acetate / 500ml of methanol mixture (capacity factor 8:2), and 500ml of ethyl acetate / methanol mixture (capacity factor 7:3) in this order, respectively, it extracted 100ml of eluates at a time. A part of each eluate fraction was taken, respectively, this was dropped at the silica gel plate for thin layer chromatography (a trade name "silica gel 60 F254", Merck manufacture) in small quantities, and after making it dry, it developed using ethyl acetate / methanol mixture (capacity factor 6:4). It extracted, when ultraviolet radiation with a wavelength of 254nm was irradiated, the plate was dried after development, it united and the eluate fraction from the column containing the component which moved to the Rf0.40 neighborhood was condensed, and it hardened by drying.

[0026] It is column chromatography like the above about the obtained solid state material (2.09g). Refine again and the eluate fraction from the column containing the component which moved to the Rf0.40 neighborhood in thin layer chromatography is extracted. When it united, condensed and hardened by drying, 1.35g of 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid was obtained as a white fine grain of a tasteless non-smell (36.3% of yield).

[0027] (2) The female panelist of 40 valuation methods of a using feeling test was divided into four groups of ten persons each, the milky lotion of the work example 1 was applied to the 1st group, the milky lotion of the comparative example 1 - the comparative example 3 was applied to the 2nd group - the 4th group, respectively, and the using feeling was evaluated about skin familiarity and smeariness. The valuation basis of a using feeling is as follows.

[0028] (Valuation basis of skin familiarity)

O : skin familiarity is good.
**: It can be called neither.
x: Skin familiarity is bad.
(Valuation basis of smeariness)
O : it is not sticky.
**: It can be called neither.
x: It is sticky.
[0029]
[Table 1]
---------- ---------- work-example comparative example Presentation (milky lotion) ---------- ---------- 1123 ---------- A. Stearic acid 2.0 2.0 2.0 2.0 Cetanol 1.0 1.0 1.0 1.0 Vaseline 2.0 2.0 2.0 2.0 Liquid paraffin 6.0 6.0 6.0 6.0 2-Ethylhexanoic Acid Sept Iles 1.0 1.0 1.0 1.0 Jojoba Oil 1.0 1.0 1.0 1.0 Squalane 2.0 2.0 2.0 2.0 Tetra 2-Ethylhexanoic Acid Pentaerythritol 3.0 3.0 3.0 3.0 Methylphenyl Polysiloxane *13.0 -3.0 - Decamethyl pentasiloxane *22.0 -2.0 - Oenotherae Biennis oil 0.5 0.5 0.5 0.5 Mono-[JIPARA methoxycinnamic acid] -2-ethylhexanoic acid glyceryl 1.5 1.5 1.5 1.5 4-tert-butyl 4'- Methoxy dibenzoylmethane 3.0 3.0 3.0 3.0 POE(10) Mono-Olate 3.0 3.0 3.0 3.0 Dibutylhydroxytoluene 0.1 0.1 0.1 0.1 Vitamin B6 Tripalmitate 0.01 0.01 0.01 0.01 Butylparaben 0.2 0.2 0.2 0.2 Proper Quantity of Flavor Optimum dose Optimum dose Optimum dose B. propylene glycol 5.0 5.0 5.0 5.0 1, 3-Butylene Glycol 2.0 2.0 2.0 2.0 2-O-alpha-D-Mono-Glucopyranosyl 6-O-Octanoyl L-ascorbic Acid 1.0 - - 1.0 Arbutin 5.0 5.0 5.0 5.0 Carboxyvinyl Polymer 0.2 0.2 0.2 0.2 Triethanolamine 0.2 0.2 0.2 0.2 Residual Purified Water Emainder Emainder Emainder ---------- ---------- Skin familiarity O7457**3322x0 3 3 1 smeariness O 9 4 9 1 ** 1 3 1 4 X 0 3 0 5----------
[0030] *1: Viscosity 50cSt (made by Shin-Etsu Chemical Co., Ltd.)
*2: Viscosity 5cSt (made by Shin-Etsu Chemical Co., Ltd.)
[0031] It compares with the milky lotion (comparative example 1) which has blended neither 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid nor silicone oil from the result of Table 1, and is only 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid. the blended milky lotion (comparative example 3) -- rather -- smeariness -- **** -- it turns out that it is. It turns out that the milky lotion (comparative example 2) of skin familiarity which blended only silicone oil is comparable, and does not improve on the other hand as compared with a comparative example 1. On the other hand, as for the milky lotion (work example 1) which blended both silicone oil with 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid, it turns out that skin familiarity is good and smeariness does not almost have it, either.
[0032] Therefore, the thing for which 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid and silicone oil are combined, Skin familiarity is good and it turns out that it can

be considered as skin external preparations also without the smeariness of 2-O-alpha-D-mono-glucopyranosyl 6-O-octanoyl L-ascorbic acid.

[0033] Next, in order to make skin external preparations of this invention more concrete, a work example is shown further. In addition, loadings show weight %. When evaluated according to the work example 1, the skin external preparations of each work example showed the same outstanding usability as a work example 1.

[0034]

Work example 2 Cream A. cetanol 0.5 Weight % vaseline 2.0 Squalane 7.0 Decamethyl Cyclopentasiloxane 10.0 [EKISE Call D-5 (5CSt; made by Shin-Etsu Chemical Co., Ltd.)] Self-emulsification type glyceryl monostearate 2.5 POE(20) sorbitan monostearin acid ester 1.5 punt thenyl ethyl ether 0.5 Jojoba oil 5.0B. propylene glycol 5.0 Glycerol 5.0 Veegum (montmorillonite) 5.0 6-O-dodeca noil 2-O-alpha-D-mono-glucopyranosyl L-ascorbic acid 1.0 Distilled Water Emainders (Process) A (Oil Phase) and B (Aqueous Phase) Complete dissolution is heated and carried out to 70 degrees C, respectively. A is added to B and it emulsifies with an emulsifier. The emulsification thing was cooled using the heat exchange mechanism, and cream was obtained.

[0035]

Work example 3 Milky lotion A. squalane 5.0 Weight % Oleyl olate 3.0 Vaseline 2.0 Sorbitan sesquioleate 0.8 POE(20) oleyl ether 1.2 Trimethylsiloxy Silicic Acid - Octamethylcyclotetrasiloxane Solution 5.0 [SSD-R-1 (100CSt; made by Shin-Etsu Chemical Co., Ltd.)]

Dimethylpolysiloxane 1.0 [KF-96A6CS (6cSt; made by Shin-Etsu Chemical Co., Ltd.)]